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NEWS	2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS	3	Feb 06	Engineering Information Encompass files have new names
NEWS	4	Feb 16	TOXLINE no longer being updated
NEWS	5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS	6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS	7	May 07	DGENE Reload
NEWS	8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS	9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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FILE 'HOME' ENTERED AT 14:20:10 ON 17 AUG 2001

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'MEDLINE' ENTERED AT 14:20:23 ON 17 AUG 2001

FILE LAST UPDATED: 16 AUG 2001 (20010816/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

```
=> s tumor (w) necrosis (w) factor or TNF
         440135 TUMOR
         200274 TUMORS
         534723 TUMOR
                   (TUMOR OR TUMORS)
         116823 NECROSIS
              1 NECROSISES
         116824 NECROSIS
                   (NECROSIS OR NECROSISES)
         490595 FACTOR
        1389241 FACTORS
        1708875 FACTOR
                   (FACTOR OR FACTORS)
          42452 TUMOR (W) NECROSIS (W) FACTOR
          32484 TNF
             94 TNFS
          32497 TNF
                   (TNF OR TNFS)
L1        47811 TUMOR (W) NECROSIS (W) FACTOR OR TNF

=> s glycosyl?
L2        41202 GLYCOSYL?

=> s l1 (s) l2
L3          217 L1 (S) L2

=> s cho (w) cells
          19199 CHO
             25 CHOS
          19205 CHO
                   (CHO OR CHOS)
        1329084 CELLS
L4        15720 CHO (W) CELLS

=> s l3 and l4
L5           11 L3 AND L4

=> d5 l5 1- ibib,abs
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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

=> d l5 1- ibib,abs
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 11 MEDLINE
ACCESSION NUMBER: 2000413020 MEDLINE
DOCUMENT NUMBER: 20390098 PubMed ID: 10770955
TITLE: Temperature-sensitive differential affinity of TRAIL for its receptors. DR5 is the highest affinity receptor.
AUTHOR: Truneh A; Sharma S; Silverman C; Khandekar S; Reddy M P; Deen K C; McLaughlin M M; Srinivasula S M; Livi G P; Marshall L A; Alnemri E S; Williams W V; Doyle M L
CORPORATE SOURCE: Department of Immunology, SmithKline Beecham Pharmaceuticals, Pennsylvania, King of Prussia, PA 19406, USA.. alem_truneh@sbphrd.com
CONTRACT NUMBER: CA78890 (NCI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jul 28) 275 (30) 23319-25.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000831

AB TRAIL is a member of the **tumor necrosis factor** (**TNF**) family of cytokines which induces apoptotic cell death in a variety of tumor cell lines. It mediates its apoptotic effects through one of two receptors, DR4 and DR5, which are members of of the **TNF** receptor family, and whose cytoplasmic regions contain death domains. In addition, TRAIL also binds to 3 "decoy" receptors, DcR2, a receptor with a truncated death domain, DcR1, a **glycosylphosphatidylinositol** -anchored receptor, and OPG a secreted protein which is also known to bind to another member of the **TNF** family, RANKL. However, although apoptosis depends on the expression of one or both of the death domain containing receptors DR4 and/or DR5, resistance to TRAIL-induced apoptosis does not correlate with the expression of the "decoy" receptors. Previously, TRAIL has been described to bind to all its receptors with equivalent high affinities. In the present work, we show, by isothermal titration calorimetry and competitive enzyme-linked immunosorbent assay, that the rank order of affinities of TRAIL for the recombinant soluble forms of its receptors is strongly temperature dependent. Although DR4, DR5, DcR1, and OPG show similar affinities for TRAIL at 4 degrees C, their rank-ordered affinities are substantially different at 37 degrees C, with DR5 having the highest affinity (K(D) </= 2 nm) and OPG having the weakest (K(D) = 400 nm). Preferentially enhanced binding of TRAIL to DR5 was also observed at the cell surface. These results reveal that the rank ordering of affinities for protein-protein interactions in general can be a strong function of temperature, and indicate that sizeable, but hitherto unobserved, TRAIL affinity differences exist at physiological temperature,

and should be taken into account in order to understand the complex physiological and/or pathological roles of TRAIL.

L5 ANSWER 2 OF 11 MEDLINE
ACCESSION NUMBER: 2000261331 MEDLINE
DOCUMENT NUMBER: 20261331 PubMed ID: 10799988
TITLE: Ammonium alters N-glycan structures of recombinant TNFR-IgG: degradative versus biosynthetic mechanisms.
AUTHOR: Gawlitzek M; Ryll T; Lofgren J; Sliwkowski M B
CORPORATE SOURCE: Process Sciences, Genentech, Inc., South San Francisco, California 94080, USA.. gawlitzek.martin@gene.com
SOURCE: BIOTECHNOLOGY AND BIOENGINEERING, (2000 Jun 20) 68 (6) 637-46.
Journal code: A6N; 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706
Entered Medline: 20000626

AB The effect of ammonium on the **glycosylation** pattern of the recombinant immunoadhesin **tumor necrosis factor**-IgG (TNFR-IgG) produced by Chinese hamster ovary cells is elucidated in this study. TNFR-IgG is a chimeric IgG fusion protein bearing one N-linked **glycosylation** site in the Fc region and three complex-type N-glycans in the **TNF**-receptor portion of each monomer. The ammonium concentration of batch suspension cultures was adjusted with glutamine and/or NH(4)Cl. The amount of galactose (Gal) and N-acetylneuraminic acid (NANA) residues on TNFR-IgG correlated in a dose-dependent manner with the ammonium concentration under which the N-linked oligosaccharides were synthesized. As ammonium increased from 1 to 15 mM, a concomitant decrease of up to 40% was observed in terminal galactosylation and sialylation of the molecule. Cell culture supernatants contained measurable beta-galactosidase and sialidase activity, which increased throughout the culture. The beta-galactosidase, but not the sialidase, level was proportional to the ammonium concentration. No loss of N-glycans was observed in incubation studies using beta-galactosidase and sialidase containing cell culture supernatants, suggesting that the ammonium effect was biosynthetic and not degradative. Several biosynthetic mechanisms were investigated. Ammonium (a weak base) is known to affect the pH of acidic intracellular compartments (e.g., trans-Golgi) as well as intracellular nucleotide sugar pools (increases UDP-N-acetylglucosamine and UDP-N-acetylgalactosamine). Ammonium might also affect the expression rates of beta1, 4-galactosyltransferase (beta1,4-GT) and alpha2,3-sialyltransferase (alpha2,3-ST). To separate these mechanisms, experiments were designed using chloroquine (changes intracellular pH) and glucosamine (increases UDP-GNAc pool [sum of UDP-GlcNAc and UDP-GalNAc]). The ammonium effect on TNFR-IgG oligosaccharide structures could be mimicked only by chloroquine, another weak base. No differences in N-**glycosylation** were found in the product synthesized in the presence of glucosamine. No differences in beta1, 4-galactosyltransferase (beta1,4-GT) and alpha2,3-sialyltransferase (alpha2,3-ST) messenger RNA

(mRNA) and enzyme levels were observed in cells cultivated in the presence
or absence of 13 mM NH(4)Cl. pH titration of endogenous CHO alpha2,3-ST and beta-1,4-GT revealed a sharp optimum at pH 6.5, the reported trans-Golgi pH. Thus, at pH 7.0 to 7.2, a likely trans-Golgi pH range in the presence of 10 to 15 mM ammonium, activities for both enzymes are reduced to 50% to 60%. Consequently, ammonium seems to alter the carbohydrate biosynthesis of TNFR-IgG by a pH-mediated effect on **glycosyltransferase** activity.

L5 ANSWER 3 OF 11 MEDLINE
ACCESSION NUMBER: 2000158975 MEDLINE
DOCUMENT NUMBER: 20158975 PubMed ID: 10692464
TITLE: Biosynthesis and post-translational processing of lectin-like oxidized low density lipoprotein receptor-1 (LOX-1). N-linked glycosylation affects cell-surface expression and ligand binding.
AUTHOR: Kataoka H; Kume N; Miyamoto S; Minami M; Murase T; Sawamura
T; Masaki T; Hashimoto N; Kita T
CORPORATE SOURCE: Department of Geriatric Medicine, Graduate School of Medicine, Kyoto University, Kyoto 606-8507, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Mar 3) 275 (9) 6573-9.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000403

AB LOX-1 (lectin-like oxidized low density lipoprotein receptor-1) is a type II membrane protein belonging to the C-type lectin family that can act as a cell-surface receptor for atherogenic oxidized low density lipoprotein (Ox-LDL) and may play crucial roles in atherogenesis. In this study, we show, by pulse-chase labeling and glycosidase digestion, that LOX-1 is synthesized as a 40-kDa precursor protein with N-linked high mannose carbohydrate chains (pre-LOX-1), which is subsequently further **glycosylated** and processed into the 48-kDa mature form within 40 min. Furthermore, when treated with an N-**glycosylation** inhibitor, tunicamycin, both **tumor necrosis factor**-alpha-activated bovine aortic endothelial cells and CHO-K1 cells stably expressing bovine LOX-1 (BLOX-1-CHO) exclusively produced a 32-kDa deglycosylated form of LOX-1. Cell enzyme-linked immunosorbent assay, flow cytometry, and immunofluorescence confocal microscopy demonstrated that the deglycosylated form of LOX-1 is not efficiently transported to the cell surface, but is retained in the endoplasmic reticulum or Golgi apparatus in **tumor necrosis factor**-alpha-activated bovine aortic endothelial cells, but not in BLOX-1-**CHO cells**. Radiolabeled Ox-LDL binding studies revealed that the deglycosylated form of LOX-1 expressed on the cell surface of BLOX-1-**CHO cells** has a reduced affinity for Ox-LDL binding. Taken together, N-linked **glycosylation** appears to play key roles in the cell-surface expression and ligand binding of LOX-1.

L5 ANSWER 4 OF 11 MEDLINE
ACCESSION NUMBER: 1999371682 MEDLINE
DOCUMENT NUMBER: 99371682 PubMed ID: 10441133
TITLE: Modulation of juxtamembrane cleavage ("shedding") of angiotensin-converting enzyme by stalk glycosylation: evidence for an alternative shedding protease.
AUTHOR: Schwager S L; Chubb A J; Scholle R R; Brandt W F; Mentele R; Riordan J F; Sturrock E D; Ehlers M R
CORPORATE SOURCE: Department of Medical Biochemistry and MRC Liver Research Centre, University of Cape Town Medical School, Observatory 7925, South Africa.
SOURCE: BIOCHEMISTRY, (1999 Aug 10) 38 (32) 10388-97.
Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990908

AB The role of juxtamembrane stalk **glycosylation** in modulating stalk cleavage and shedding of membrane proteins remains unresolved, despite reports that proteins expressed in **glycosylation** -deficient cells undergo accelerated proteolysis. We have constructed stalk **glycosylation** mutants of angiotensin-converting enzyme (ACE), a type I ectoprotein that is vigorously shed when expressed in Chinese hamster ovary cells. Surprisingly, stalk **glycosylation** did not significantly inhibit release. Introduction of an N-linked glycan directly adjacent to the native stalk cleavage site resulted in a 13-residue, proximal displacement of the cleavage site, from the Arg-626/Ser-627 to the Phe-640/Leu-641 bond. Substitution of the wild-type stalk with a Ser-/Thr-rich sequence known to be heavily O-**glycosylated** produced a mutant (ACE-JGL) in which this chimeric stalk was partially O-**glycosylated**; incomplete **glycosylation** may have been due to membrane proximity. Relative to levels of cell-associated ACE-JGL, rates of basal, unstimulated release of ACE-JGL were enhanced compared with wild-type ACE. ACE-JGL was cleaved at an Ala/Thr bond, 14 residues from the membrane. Notably, phorbol ester stimulation and TAPI (a peptide hydroxamate) inhibition of release-universal characteristics of regulated ectodomain shedding-were significantly blunted for ACE-JGL, as was a formerly undescribed transient stimulation of ACE release by 3, 4-dichloroisocoumarin. These data indicate that (1) stalk **glycosylation** modulates but does not inhibit ectodomain shedding; and (2) a Ser-/Thr-rich, O-**glycosylated** stalk directs cleavage, at least in part, by an alternative shedding protease, which may resemble an activity recently described in **TNF**-alpha convertase null cells [Buxbaum, J. D., et al. (1998) J. Biol. Chem. 273, 27765-27767].

L5 ANSWER 5 OF 11 MEDLINE
ACCESSION NUMBER: 1999324197 MEDLINE
DOCUMENT NUMBER: 99324197 PubMed ID: 10393956

TITLE: The mast cell **tumor necrosis factor** alpha response to FimH-expressing Escherichia coli is mediated by the **glycosylphosphatidylinositol**-anchored molecule CD48.

AUTHOR: Malaviya R; Gao Z; Thankavel K; van der Merwe P A; Abraham S N

CORPORATE SOURCE: Department of Pathology and Microbiology, Duke University Medical Center, Durham, NC 27710, USA.

CONTRACT NUMBER: AI 35678 (NIAID)
DK 50814 (NIDDK)

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Jul 6) 96 (14) 8110-5.
Journal code: PV3; 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826

AB Mast cells are well known for their harmful role in IgE-mediated hypersensitivity reactions, but their physiological role remains a mystery. Several recent studies have reported that mast cells play a critical role in innate immunity in mice by releasing **tumor necrosis factor** alpha (**TNF**-alpha) to recruit neutrophils to sites of enterobacterial infection. In some cases, the mast cell **TNF**-alpha response was triggered when these cells directly bound FimH on the surface of Escherichia coli. We have identified CD48, a **glycosylphosphatidylinositol**-anchored molecule, to be the complementary FimH-binding moiety in rodent mast cell membrane fractions. We showed that (i) pretreatment of mast cell membranes with antibodies to CD48 or phospholipase C inhibited binding of FimH+ E. coli, (ii) FimH+ E. coli but not a FimH- derivative bound isolated CD48 in a mannose-inhibitable manner, (iii) binding of FimH+ bacteria to Chinese hamster ovary (**CHO**) **cells** was markedly increased when these cells were transfected with CD48 cDNA, and (iv) antibodies to CD48 specifically blocked the mast cell **TNF**-alpha response to FimH+ E. coli. Thus, CD48 is a functionally relevant microbial receptor on mast cells that plays a role in triggering inflammation.

L5 ANSWER 6 OF 11 MEDLINE

ACCESSION NUMBER: 1999214204 MEDLINE
DOCUMENT NUMBER: 99214204 PubMed ID: 10196211

TITLE: Recombinant glycoproteins that inhibit complement activation and also bind the selectin adhesion molecules.

AUTHOR: Rittershaus C W; Thomas L J; Miller D P; Picard M D; Geoghegan-Barek K M; Scesney S M; Henry L D; Sen A C; Bertino A M; Hannig G; Adari H; Mealey R A; Gosselin M L; Couto M; Hayman E G; Levin J L; Reinhold V N; Marsh H C Jr

CORPORATE SOURCE: Avant Immunotherapeutics, Inc., Needham, Massachusetts 02494-2725, USA.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Apr 16) 274 (16) 11237-44.
Journal code: HIV; 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990517

AB Soluble human complement receptor type 1 (sCR1, TP10) has been expressed in Chinese hamster ovary (CHO) DUKX-B11 cells and shown to inhibit the classical and alternative complement pathways in vitro and in vivo. A truncated version of sCR1 lacking the long homologous repeat-A domain (LHR-A) containing the C4b binding site has similarly been expressed and designated sCR1[desLHR-A]. sCR1[desLHR-A] was shown to be a selective inhibitor of the alternative complement pathway in vitro and to function in vivo. In this study, sCR1 and sCR1[desLHR-A] were expressed in CHO LEC11 cells with an active alpha(1,3)-fucosyltransferase, which makes possible the biosynthesis of the sialyl-Lewisx (sLex) tetrasaccharide (NeuNAcalpha2-3Galbeta1-4(Fucalpha1-3)GlcNAc) during post-translational **glycosylation**. The resulting glycoproteins, designated sCR1sLex and sCR1[desLHR-A]sLex, respectively, retained the complement regulatory activities of their DUKX B11 counterparts, which lack alpha(1-3)-fucose. Carbohydrate analysis of purified sCR1sLex and sCR1[desLHR-A]sLex indicated an average incorporation of 10 and 8 mol of sLex/mol of glycoprotein, respectively. sLex is a carbohydrate ligand for the selectin adhesion molecules. sCR1sLex was shown to specifically bind **CHO cells** expressing cell surface E-selectin. sCR1[desLHR-A]sLex inhibited the binding of the monocytic cell line U937 to human aortic endothelial cells, which had been activated with **tumor necrosis factor**-alpha to up-regulate the expression of E-selectin. sCR1sLex inhibited the binding of U937 cells to surface-adsorbed P-selectin-IgG. sCR1sLex and sCR1[desLHR-A]sLex have thus demonstrated both complement regulatory activity and the capacity to bind selectins and to inhibit selectin-mediated cell adhesion in vitro.

L5 ANSWER 7 OF 11 MEDLINE
ACCESSION NUMBER: 1998070475 MEDLINE
DOCUMENT NUMBER: 98070475 PubMed ID: 9407058
TITLE: Multimer formation and ligand recognition by the long pentraxin PTX3. Similarities and differences with the short pentraxins C-reactive protein and serum amyloid P component.
AUTHOR: Bottazzi B; Vouret-Craviari V; Bastone A; De Gioia L; Matteucci C; Peri G; Spreafico F; Pausa M; D'Ettorre C; Gianazza E; Tagliabue A; Salmona M; Tedesco F; Introna M; Mantovani A
CORPORATE SOURCE: From the Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea 62, 20157 Milano, Italy.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Dec 26) 272 (52) 32817-23.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980123

AB PTX3 is a prototypic long pentraxin consisting of a C-terminal 203-amino acid pentraxin-like domain coupled with an N-terminal 178-amino acid unrelated portion. The present study was designed to characterize the structure and ligand binding properties of human PTX3, in comparison with the classical pentraxins C-reactive protein and serum amyloid P component.

Sequencing of Chinese hamster ovary cell-expressed PTX3 revealed that the mature secreted protein starts at residue 18 (Glu). Lectin binding and treatment with N-glycosidase F showed that PTX3 is N-**glycosylated**, sugars accounting for 5 kDa of the monomer mass (45 kDa). Circular dichroism analysis indicated that the protein consists predominantly of beta-sheets with a minor alpha-helical component. While in gel filtration the protein is eluted with a molecular mass of congruent with900 kDa, gel electrophoresis using nondenaturing, nonreducing conditions revealed that PTX3 forms multimers predominantly of 440 kDa apparent molecular mass, corresponding to decamers, and that disulfide bonds are required for multimer formation. The ligand binding properties of PTX3 were then examined. As predicted based on modeling, inductive coupled plasma/atomic emission spectroscopy showed that PTX3 does not have coordinated Ca2+. Unlike the classical pentraxins CRP and SAP, PTX3 did not bind phosphoethanolamine, phosphocholine, or high pyruvate agarose. PTX3 in solution, bound to immobilized C1q, but not C1s, and, reciprocally, C1q bound to immobilized PTX3. Binding of PTX3 to C1q is specific and saturable with a Kd 7.4 x 10(-8) M as determined by solid phase binding assay. The Chinese hamster ovary cell-expressed pentraxin domain bound C1q when multimerized. Thus, as predicted on the basis of computer modeling, the prototypic long pentraxin PTX3 forms multimers, which differ from those formed by classical pentraxins in terms of protomer composition and requirement for disulfide bonds, and does not recognize CRP/SAP ligands. The capacity to bind C1q, mediated by the pentraxin domain, is consistent with the view that PTX3, produced in tissues by endothelial cells or macrophages in response to interleukin-1 and **tumor necrosis factor**, may act as a local regulator of innate immunity.

L5 ANSWER 8 OF 11 MEDLINE
ACCESSION NUMBER: 96172469 MEDLINE
DOCUMENT NUMBER: 96172469 PubMed ID: 8590318
TITLE: Identification of two forms (31-33 and 48 kD) of the urinary soluble p55 **tumor necrosis factor** receptor that are differentially N- and O-**glycosylated**.
AUTHOR: Corti A; Merli S; Bagnasco L; D'Ambrosio F; Marino M; Cassani G
CORPORATE SOURCE: Molecular Immunology and Biochemistry Unit, Tecnogen ScpA, Piana di Monte Verna, Italy.
SOURCE: JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, (1995 Feb) 15 (2) 143-52.
Journal code: CD4; 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960404
Last Updated on STN: 19960404
Entered Medline: 19960325

AB The structure and the activity of urinary soluble **TNF** receptor type 1 (sTNF-R1), isolated from the urine of normal individuals, has been characterized and compared with that of recombinant sTNF-R1 expressed in **CHO cells** and with that of a nonglycosylated form expressed in Escherichia coli. Urinary sTNF-R1 was resolved in a major band of 31-33 kD and in a 48 kD band (less than 5% of total) by reducing SDS-PAGE; CHO sTNF-R1 was resolved in two bands of 29 and 31 kD. All bands were recognized by various anti-sTNF-R1 antibodies as well as by **TNF**-alpha in western and ligand blotting assays. No cross-reaction was observed with anti-**TNF**-R2 antibodies. N- and O-**glycosylation** studies indicated that (1) the 29-31 kD recombinant form as well as the 31-33 kD urinary form are N-**glycosylated**; (2) the differences between the 29-31 and 31-33 kD recombinant and natural products are mainly related to differences in the N-linked sugar content; and (3) the 48 kD sTNF-R1 isolated from urine also contains O-linked sugars. The urinary sTNF-R1 antigen mixture was able to inhibit **TNF**-alpha cytotoxicity with a potency comparable to that of nonglycosylated E. coli sTNF-R1. At variance, urinary sTNF-R1 was able to inhibit **TNF**-beta sevenfold more efficiently than E. coli sTNF-R1. In conclusion, two subtypes of sTNF-R1 have been isolated from urine: a main N-**glycosylated** form of 31-33 kD and a N- and O-**glycosylated** form of 48 kD that appears to be a minor constituent of the urinary sTNF-R1 antigen.

L5 ANSWER 9 OF 11 MEDLINE
ACCESSION NUMBER: 94286533 MEDLINE
DOCUMENT NUMBER: 94286533 PubMed ID: 8016076
TITLE: Specific human granulocyte-macrophage colony-stimulating factor antagonists.
AUTHOR: Hercus T R; Bagley C J; Cambareri B; Dottore M; Woodcock J M; Vadas M A; Shannon M F; Lopez A F
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science, Adelaide, South Australia.
CONTRACT NUMBER: CA 45822 (NCI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Jun 21) 91 (13) 5838-42. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940810
Last Updated on STN: 19980206
Entered Medline: 19940728

AB Human granulocyte-macrophage colony-stimulating factor (GM-CSF) is a pleiotropic hemopoietic growth factor and activator of mature myeloid cell function. We have previously shown that residue 21 in the first helix of GM-CSF plays a critical role in both biological activity and high-affinity

receptor binding. We have now generated analogues of GM-CSF mutated at residue 21, expressed them in Escherichia coli, and examined them for binding, agonistic, and antagonistic activities. Binding experiments showed that GM E21A, E21Q, E21F, E21H, E21R, and E21K bound to the GM-CSF receptor alpha chain with a similar affinity to wild-type GM-CSF and had lost high-affinity binding to the GM-CSF receptor alpha-chain-common beta-chain complex. From these mutants, only the charge reversal mutants E21R and E21K were completely devoid of agonistic activity. Significantly we found that E21R and E21K antagonized the proliferative effect of GM-CSF on the erythroleukemic cell line TF-1 and primary acute myeloid leukemias, as well as GM-CSF-mediated stimulation of neutrophil superoxide production. This antagonism was specific for GM-CSF in that no antagonism of interleukin 3-mediated TF-1 cell proliferation or **tumor necrosis factor** alpha-mediated stimulation of neutrophil superoxide production was observed. E. coli-derived GM E21R and E21K were effective antagonists of both nonglycosylated and **glycosylated** wild-type GM-CSF. These results show that low-affinity GM-CSF binding can be dissociated from receptor activation and have potential clinical significance for the management of inflammatory diseases and certain leukemias where GM-CSF plays a pathogenic role.

L5 ANSWER 10 OF 11 MEDLINE
ACCESSION NUMBER: 93311995 MEDLINE
DOCUMENT NUMBER: 93311995 PubMed ID: 8323280
TITLE: N-linked sugar chain structure of recombinant human lymphotoxin produced by **CHO cells**: the functional role of carbohydrate as to its lectin-like character and clearance velocity.
AUTHOR: Fukushima K; Watanabe H; Takeo K; Nomura M; Asahi T; Yamashita K
CORPORATE SOURCE: Department of Biochemistry, Sasaki Institute, Tokyo, Japan.
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1993 Jul) 304 (1) 144-53.
Journal code: 6SK; 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
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AB Recombinant human lymphotoxin (rhLT) produced by **CHO cells** transfected with human LT genomic DNA was purified to homogeneity, but approximately 5% of the molecules were devoid of the last two amino terminal residues. A peptide N-**glycosylated** at Asn62 (Tr-45) and one partially O-**glycosylated** at Thr7 (Tr-14) on cleavage with trypsin were separated by reverse phase HPLC. The N-linked sugar chains of Tr-45 were released quantitatively as oligosaccharides on hydrazinolysis (100 degrees C, 8 h), followed by N-acetylation. After being reduced with either NaB3H4 or NaB2H4, their structures were determined by a combination of serial lectin affinity chromatography, exoglycosidase digestion, and methylation analysis: 82.7% of the sugar

chains occur as biantennary complex-type sugar chains, the remainder being
C-2 and C-2,4/C-2,6 branched triantennary, and C-2,4 and C-2,6 branched tetraantennary complex-type sugar chains with a fucosylated mannose core. Their sialic acid residues occur only as the Neu5Ac alpha 2-->3Gal group. The clearance velocity from the bloodstream dramatically increased with desialylation, and rhLT tends to have accumulated in the kidney, indicating that there may exist other mechanisms for clearance from the circulation besides the galactose-binding protein in hepatocytes and the filtration system of the kidney. Desialylated rhLT showed a lectin-like binding character to uromodulin similar to that of **tumor necrosis factor**, although intact rhLT did not. The interaction between desialylated rhLT and uromodulin was inhibited by N,N'-diacetylchitobiose and [Man alpha 1-->6(Man alpha 1-->3)Man alpha 1-->6](Man alpha 1-->2Man alpha 1-->3)Man beta 1-->4GlcNAc beta 1-->4GlcNAc-->Asn. These results indicate that the lectin-like domain of rhLT is exposed on its desialylation.

L5 ANSWER 11 OF 11 MEDLINE
ACCESSION NUMBER: 85242112 MEDLINE
DOCUMENT NUMBER: 85242112 PubMed ID: 2989794
TITLE: Molecular cloning of mouse tumour necrosis factor cDNA and its eukaryotic expression.
AUTHOR: Fransen L; Muller R; Marmenout A; Tavernier J; Van der Heyden J; Kawashima E; Chollet A; Tizard R; Van Heuverswyn H; Van Vliet A; +
SOURCE: NUCLEIC ACIDS RESEARCH, (1985 Jun 25) 13 (12) 4417-29. Journal code: O8L; 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
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AB Tumour necrosis factor (**TNF**), released by induced macrophages, causes tumour necrosis in animals and kills preferentially transformed cells in vitro. mRNA induced in the established mouse monocytic PU 5.1.8 cell line by lipopolysaccharide, was converted into double-stranded cDNA and cloned in the pAT153 vector. Recombinant plasmids were screened by plus-minus hybridization and **TNF**-specific oligonucleotide probes constructed on the basis of partial amino acid sequences of rabbit **TNF**. A series of **TNF** specific clones were identified and confirmed by hybrid selection of mouse **TNF**-specific mRNA. The sequence codes for a 235 amino acids long polypeptide, of which 156 amino acids presumably correspond to the mature product. It can be concluded that mature mouse **TNF** is a **glycosylated** dimer. Biologically active **TNF** was secreted by both Cos-I and **CHO-cells** transfected with the chimaeric expression vector pSV2d2-mTNF containing the coding region of the mouse **TNF** cDNA gene.

=> s l1 (p) l2
L6 217 L1 (P) L2

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=> s l4 and l6
L7          11 L4 AND L6

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.90       8.05

STN INTERNATIONAL LOGOFF AT 14:32:02 ON 17 AUG 2001
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